

Amendments to the Specification:

Please replace paragraph [0014] with the following rewritten paragraph:

[0014] According to one aspect of the present invention, a detector for detecting and simultaneously diagnosing at least one subtype of human papilloma viruses (HPV) contained in a biological sample, comprises: a carrier, a plurality of micro-dots immobilized on the carrier, wherein each micro-dot is for identifying one particular HPV subtype, and the HPV subtype is one selected from a group consisting of (HPV 6, HPV 11, HPV 16, HPV 18, HPV 26, HPV 31, HPV 32, HPV 33, HPV 35, HPV 37, HPV 39, HPV 42, HPV 43, HPV 44, HPV 45, HPV 51, HPV 52, HPV 53, HPV 54, HPV 55, HPV 56, HPV 58, HPV 59, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV CP8304, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8); and at least one oligonucleotide sequence contained in each the micro-dot that is specific to the one particular HPV subtype, wherein the at least one oligonucleotide sequence serves as a detection probe that hybridizes specifically with an L1 gene sequence of the one particular HPV subtype to form a hybridization complex as a detection indicator, so that each micro-dot identifies one particular HPV subtype via a corresponding oligonucleotide of the one particular HPV subtype, and thereby detecting and simultaneously identifying subtypes of human papilloma viruses.

Please replace paragraph [0015] with the following rewritten paragraph:

[0015] In accordance with the present invention, the at least one oligonucleotide that hybridizes specifically with an L1 gene sequence of the one particular HPV subtype is respectively chosen from the following list for each HPV subtype: (SEQ ID NO:1-SEQ ID NO:12) for HPV 6, (SEQ ID NO:13-SEQ ID NO:24) for HPV 11, (SEQ ID NO:25-SEQ ID NO:36) for HPV 16, (SEQ ID NO:37-SEQ ID NO:48) for HPV 18, (SEQ ID NO:49-SEQ ID NO:58) for HPV 26, (SEQ ID NO:59-SEQ ID NO:68) for HPV 31, (SEQ ID NO:69-SEQ ID NO:79) for HPV 32, (SEQ ID NO:80-SEQ ID NO:90) for HPV 33, (SEQ ID NO:91-SEQ ID NO:100) for HPV 35, (SEQ ID NO:101-SEQ ID NO:112) for HPV 37, (SEQ ID NO:113-SEQ ID NO:123) for HPV 39, (SEQ ID NO:124-SEQ ID NO:133) for HPV 42, (SEQ ID NO:134-SEQ ID NO:143) for HPV 43, (SEQ ID NO:144-SEQ ID NO:154) for HPV 44, (SEQ ID NO:155-SEQ ID NO:165) for HPV 45, (SEQ ID NO:166-SEQ ID NO:177) for HPV 51, (SEQ

ID NO:178-SEQ ID NO:189) for HPV 52, (SEQ ID NO:190-SEQ ID NO:199) for HPV 53, (SEQ ID NO:200-SEQ ID NO:209) for HPV 54, (SEQ ID NO:210-SEQ ID NO:218) for HPV 55, (SEQ ID NO:219-SEQ ID NO:228) for HPV 56, (SEQ ID NO:229-SEQ ID NO:239) for HPV 58, (SEQ ID NO:240-SEQ ID NO:250) for HPV 59, (SEQ ID NO:251-SEQ ID NO:261) for HPV 61, (SEQ ID NO:262-SEQ ID NO:272) for HPV 62, (SEQ ID NO:273-SEQ ID NO:283) for HPV 66, (SEQ ID NO:284-SEQ ID NO:294) for HPV 67, (SEQ ID NO:295-SEQ ID NO:305) for HPV 68, (SEQ ID NO:306-SEQ ID NO:316) for HPV 69, (SEQ ID NO:317-SEQ ID NO:328) for HPV 70, (SEQ ID NO:329-SEQ ID NO:341) for HPV 72, (SEQ ID NO:342-SEQ ID NO:353) for HPV 74, (SEQ ID NO:354-SEQ ID NO:362) for HPV 82, (SEQ ID NO:363-SEQ ID NO:374) for HPV CP8061, (SEQ ID NO:375-SEQ ID NO:386) for HPV CP8304 CP8034, (SEQ ID NO:387-SEQ ID NO:397) for HPV L1AE5, (SEQ ID NO:398-SEQ ID NO:408) for HPV MM4, (SEQ ID NO:409-SEQ ID NO:419) for HPV MM7, and (SEQ ID NO:420-SEQ ID NO:429) for HPV MM8.

Please replace paragraph [0020] with the following rewritten paragraph:

[0020] Preferably, the detector further comprises a micro-dot containing a glyceraldehyde-3-phosphate dehydrogenase Glutaldehyde-3-phosphodehydrogenase (GAPDH) gene, which is used as an internal control.

Please replace paragraph [0028] with the following rewritten paragraph:

[0028] According to another aspect of the present invention, a probe which hybridizes to nucleic acid from an HPV subtype, the probe being selected from the group consisting of: SEQ ID NO:1-SEQ ID NO:12 and sequences fully complementary thereto, which hybridize with HPV 6; SEQ ID NO:13-SEQ ID NO:24 and sequences fully complementary thereto, which hybridize with HPV 11; SEQ ID NO:25-SEQ ID NO:36 and sequences fully complementary thereto, which hybridize with HPV 16; SEQ ID NO:37-SEQ ID NO:48 and sequences fully complementary thereto, which hybridize with HPV 18; SEQ ID NO:49-SEQ ID NO:58 and sequences fully complementary thereto, which hybridize with HPV 26; SEQ ID NO:59-SEQ ID NO:68 and sequences fully complementary thereto, which hybridize with HPV 31; SEQ ID NO:69-SEQ ID NO:79 and sequences fully complementary thereto, which hybridize with HPV 32; SEQ ID NO:80-SEQ ID NO:90 and sequences fully complementary thereto, which hybridize

with HPV 33; SEQ ID NO:91-SEQ ID NO:100 and sequences fully complementary thereto, which hybridize with HPV 35; SEQ ID NO:101-SEQ ID NO:112 and sequences fully complementary thereto, which hybridize with HPV 37; SEQ ID NO:113-SEQ ID NO:123 and sequences fully complementary thereto, which hybridize with HPV 39; SEQ ID NO:124-SEQ ID NO:133 and sequences fully complementary thereto, which hybridize with HPV 42; SEQ ID NO:134-SEQ ID NO:143 and sequences fully complementary thereto, which hybridize with HPV 43; SEQ ID NO:144-SEQ ID NO:154 and sequences fully complementary thereto, which hybridize with HPV 44; SEQ ID NO:155-SEQ ID NO:165 and sequences fully complementary thereto, which hybridize with HPV 45; SEQ ID NO:166-SEQ ID NO:177 and sequences fully complementary thereto, which hybridize with HPV 51; SEQ ID NO:178-SEQ ID NO:189 and sequences fully complementary thereto, which hybridize with HPV 52; SEQ ID NO:190-SEQ ID NO:199 and sequences fully complementary thereto, which hybridize with HPV 53; SEQ ID NO:200-SEQ ID NO:209 and sequences fully complementary thereto, which hybridize with HPV 54; SEQ ID NO:210-SEQ ID NO:218 and sequences fully complementary thereto, which hybridize with HPV 55; SEQ ID NO:219-SEQ ID NO:228 and sequences fully complementary thereto, which hybridize with HPV 56; SEQ ID NO:229-SEQ ID NO:239 and sequences fully complementary thereto, which hybridize with HPV 58; SEQ ID NO:240-SEQ ID NO:250 and sequences fully complementary thereto, which hybridize with HPV 59; SEQ ID NO:251-SEQ ID NO:261 and sequences fully complementary thereto, which hybridize with HPV 61; SEQ ID NO:262-SEQ ID NO:272 and sequences fully complementary thereto, which hybridize with HPV 62; SEQ ID NO:273-SEQ ID NO:283 and sequences fully complementary thereto, which hybridize with HPV 66; SEQ ID NO:284-SEQ ID NO:294 and sequences fully complementary thereto, which hybridize with HPV 67; SEQ ID NO:295-SEQ ID NO:305 and sequences fully complementary thereto, which hybridize with HPV 68; SEQ ID NO:306-SEQ ID NO:316 and sequences fully complementary thereto, which hybridize with HPV 69; SEQ ID NO:317-SEQ ID NO:328 and sequences fully complementary thereto, which hybridize with HPV 70; SEQ ID NO:329-SEQ ID NO:341 and sequences fully complementary thereto, which hybridize with HPV 72; SEQ ID NO:342-SEQ ID NO:353 and sequences fully complementary thereto, which hybridize with HPV 74; SEQ ID NO:354-SEQ ID NO:362 and sequences fully complementary

thereto, which hybridize with HPV 82; SEQ ID NO:363-SEQ ID NO:374 and sequences fully complementary thereto, which hybridize with HPV CP8061; SEQ ID NO:375-SEQ ID NO:386 and sequences fully complementary thereto, which hybridize with HPV-CP8304-CP8034; SEQ ID NO:387-SEQ ID NO:397 and sequences fully complementary thereto, which hybridize with HPV L1AE5; SEQ ID NO:398-SEQ ID NO:408 and sequences fully complementary thereto, which hybridize with HPV MM4; SEQ ID NO:409-SEQ ID NO:419 and sequences fully complementary thereto, which hybridize with HPV MM7; and SEQ ID NO:420-SEQ ID NO:429 and sequences fully complementary thereto, which hybridize with HPV MM8.

Please replace paragraph [0046] with the following rewritten paragraph:

[0046] The PCR fragments synthesized by the primer sets MY11/MY09 in the L1 region are about 450 bp in length and had been published. The sequences of the fragments for each HPV subtype described in the invention are publicly available, for example, from the National Center for Biotechnology Information (NCBI) (e.g., www.ncbi.nih.gov). The 39 HPV subtypes identified in the invention includes HPV 6, HPV 11, HPV 16, HPV 18, HPV 26, HPV 31, HPV 32, HPV 33, HPV 35, HPV 37, HPV 39, HPV 42, HPV 43, HPV 44, HPV 45, HPV 51, HPV 52, HPV 53, HPV 54, HPV 55, HPV 56, HPV 58, HPV 59, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV-CP8304-CP8034, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8. The original NCBI Accession number and the loci of the PCR fragments synthesized by the primer sets MY11/MY09 for different HPV subtypes are listed in Table 1:

Please replace the table section at page 40, line 7 with the following rewritten section:

HPV CP8304 CP8034

SEQ ID NO	5' → 3'	Locus in HPV <u>CP8034-CP8304</u>
375	CAGCTACATCTGCTG	92 – 106
376	GCTACATCTGCTGCTGCAGA	94 – 113
377	ACATCTGCTGCTGCAGAACATA	97 – 118
378	TGCTGCAGAACATAACAAGGCCT	105 – 124
379	GCTGCAGAACATAACAAGGCCTC	106 – 125
380	CAGAACATAACAAGGCCTCAAC	110 – 129
381	TAAAATACAGTTAACACCAGAAA	189 - 211
382	CAAGGCACTGTTGGATGAT	237 – 255
383	TGTGTTGCCACCTCCTCCACCAGTT	267 – 292
384	ATATCGCTTTTACAGTCTCGG	303 – 324
385	GGGTGCTGCTGCCCTGCGCCC	342 – 363
386	TTATGCCGACATGTCA	375 – 390

Please replace paragraph [0090] with the following rewritten paragraph:

[0090] As described in the above, the probes will hybridize specifically with the L1 gene sequence of the corresponding HPV subtype. Preferably, the probes have a length between 15-30 bases. The oligonucleotide sequences contained in each micro-dot 12 serve as a detection probe, which hybridizes specifically with the L1 gene sequence of the particular HPV subtype to form a hybridization complex as a detection indicator. Therefore, each micro-dot 12 identifies a specific HPV subtype via a corresponding oligonucleotide of the specific HPV subtype, and thereby detecting and simultaneously identifying subtypes of human papilloma viruses. The sequences of the oligonucleotides provided by the present invention are specific to the epidemics of human papilloma viruses. The detector 10 is able to simultaneously identify 39 different HPV subtype that are HPV 6, HPV 11, HPV 16, HPV 18, HPV 26, HPV 31, HPV 32, HPV 33, HPV 35, HPV 37, HPV 39, HPV 42, HPV 43, HPV 44, HPV 45, HPV 51, HPV 52, HPV 53, HPV 54,

HPV 55, HPV 56, HPV 58, HPV 59, HPV 61, HPV 62, HPV 66, HPV 67, HPV 68, HPV 69, HPV 70, HPV 72, HPV 74, HPV 82, HPV CP8061, HPV CP8304 -CP8034, HPV L1AE5, HPV MM4, HPV MM7 and HPV MM8. Furthermore, the detector 10 includes the micro-dot 12 containing a Glutaldehyde-3-phosphodehydrogenase—Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) gene, which is used as an internal control.

Please replace paragraph [0098] with the following rewritten paragraph:

[0098] The subtype of human papilloma viruses identified by each dot of the micro-dots 22 is illustrated in Fig. 2(b). SC (system control) presents the PCR product amplified from any subtype of human papilloma viruses and biotin-contained primer. NC (negative control) presents the plants DNA fragment irrelevant to HPV. ICIN-(internal control) presents the sequence 5'-gcccgagactgtgggtggcag-3' (SEQ ID NO 470) of the housekeeping gene, Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH). In sum, the biochip 20 provided in the present invention is able to detect and simultaneously identify 39 different HPV subtypes contained in the biological sample.

Please replace paragraph [00103] with the following rewritten paragraph:

[00103] 2.1 Glyceraldehyde-3-phosphate dehydrogenase Glutaldehyde-3-phosphodehydrogenase-(GAPDH) gene is used as the internal control of the polymerase chain reactions so that it could help confirm whether the detecting protocols are precisely followed. The steps are described according to the following steps 2.1.1 to 2.1.3.

2.1.1 Mixing the following components:

Reagent	Stock	amount	Final concentration
Sterile H ₂ O		2.6	
10X <i>Taq</i> Buffer		0.5	1X <i>Taq</i> Buffer
dNTP	2.5 mM	0.4	200 μM
Template		1	
GAP241-5 ¹⁾ primer	10 pmol/μl	0.2	0.4 pmol/μl
GAP241-3 ²⁾ primer	10 pmol/μl	0.2	0.4 pmol/μl
ProTaq (PROTECH)	5 U/μl	0.1	0.1 U/μl
Total volume (μl)		5	

1) Gap241-5 (SEQ ID NO 471): CCACCAACTGCTTAGCACCCC

2) Gap241-3 (SEQ ID NO 472): TGCAGCGTACTCCCCACATCA

3) The proper amount of mineral oil is added to prevent the evaporation.

2.1.2 The polymerase chain reaction is performed according to the following programs.

Program 1	Program 2	Program 3
94°C , 15 seconds		
94°C ,	57°C ,	72°C ,
3 minutes	1 minute	5 minutes
72°C , 30 seconds		
40 cycles		

2.1.3 The product of the polymerase chain reaction is analyzed in 2.5% agarose/EtBr (0.5×TBE).